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# Adherence in multiple sclerosis (ADAMS): Classification, relevance, and research needs. A meeting report

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## Abstract

**Background:** Adherence to medical interventions is a global problem. With an increasing amount of partially effective but expensive drug treatments adherence is increasingly relevant in multiple sclerosis (MS). Perceived lack of efficacy and side effects as well as neuropsychiatric factors such as forgetfulness, fatigue and depression are major determinants. However, research on adherence to behavioural interventions as part of rehabilitative interventions has only rarely been studied.

**Methods:** In a one-day meeting health researchers as well as patient representatives and other stakeholders discussed adherence issues in MS and developed a general draft research agenda within a focus group session.

**Results:** The focus group addressed four major areas: (1) focussing patients and their informal team; (2) studying health care professionals; (3) comparing practice across cultures; and (4) studying new adherence interventions.

**Conclusions:** A focus on patient preferences as well as a non-judgemental discussion on adherence issues with patients should be at the core of adherence work.

**Keywords:** Disease-modifying therapies, multiple sclerosis, rehabilitation, adherence

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## Introduction

The importance of patient adherence for optimizing the benefits from medical products and interventions has been emphasized by World Health Organization and European Union initiatives.<sup>1,2</sup> Approximately 50% of patients with medical conditions do not adhere to treatment; although influenced by specific disease and type of treatment, adherence rates are even lower among patients with chronic illness.<sup>1-3</sup> With frequent approvals of easily administered but potentially risky new treatments in multiple sclerosis (MS), exploring how patients' orientate themselves to decision-making processes about treatment as well as their subsequent treatment adherence becomes increasingly important. To date, most treatment-related research in MS has explored factors associated with medication adherence. Medications comprise an important part of treatment, but behavioural interventions have demonstrated effectiveness and are

increasingly utilized. Consequently, adherence to behavioural interventions such as physical rehabilitation and psychotherapy is also important for sustaining patients' quality of life and autonomy. Within this context, across all medical conditions very few effective interventions to improve adherence exist, and focussed, interdisciplinary research is needed.<sup>4</sup>

An exploratory meeting (17 April 2013) convened under the auspices of the European Rehabilitation in MS (RIMS) network was held with clinicians, researchers, patient representatives, and other stakeholders. The goal was to summarize the current knowledge on adherence in MS and to identify first steps towards developing an ongoing research agenda.

The first part of the meeting consisted of participants' short presentations about adherence in general and in

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MS. Within the meeting, a structured focus group with the participants ( $n=20$ ) was used to compile future research and care prospects for adherence in MS (for detailed group information see participant list below). By including patients, scientists, and public involvement, the group made an effort to incorporate multiple perspectives. A list of core questions was devised by the facilitators (PB and WC) and the focus group lasted for 90 minutes.

### Summary of presentations

The terms compliance, adherence, persistence, and concordance have often been used interchangeably in the literature on medicines adherence. However, these terms have different meanings and, to some extent, reflect different perspectives and priorities in relation to the overall process of prescribing and medicines usage. The term compliance has been associated with a paternalistic healthcare approach based on the concept that patients need to follow rules. When patients' actions do not match the expectations placed on them by health professionals they are non-compliant. Adherence allows for the active agreement, consent, and involvement of the patient who is prescribed medication. Concordance was introduced to describe a collaborative or shared process of discussion and decision-making between the patient and healthcare provider. However, even after 15 years of research and practice, the efficacy of shared decision-making remains difficult to determine.<sup>5</sup> The ADAMS group suggests the term 'adherence', as it offers the most practical term in the field, integrating concordance, and offering approaches for evaluation and measurement. Non-adherence may be subdivided into intentional and non-intentional facets. Furthermore, non-adherence can be split into inconsistent implementation (e.g. missing doses) and treatment interruption or stopping, which is also referred to as lack of treatment persistence.<sup>2</sup> These differences are often not clearly delineated in MS adherence research studies.

Various theoretical models have been developed to better understand behaviour change and treatment adherence in healthcare settings. However, none of these models alone captures all aspects of behaviour change and treatment adherence. The WHO report<sup>1</sup> addresses five major domains being relevant: condition-related, patient-related, treatment-related, socio-economic as well as health system-related factors. These factors need to be explored when modelling a behaviour change intervention. Recently, the British National Institute for Health and Care Excellence (NICE) has issued a guideline on individual behaviour change approaches.<sup>6</sup>

In MS, drug treatment discontinuation rates range from 16% up to 50% or higher depending on the methodology used in studies, including length and manner of adherence monitoring (for review see elsewhere<sup>7,8</sup>). In addition, though there is no agreed gold standard for the percentage of doses needed for therapeutic effectiveness, 1 in 5 patients continuing to take medication miss more than 20% of their prescribed doses.<sup>9</sup> Major reasons for inconsistent use may be non-intentional (e.g. forgetfulness, general fatigue, emotional distress). Side effects also play an important role. Major reasons for treatment discontinuation include adverse events and perceived lack of treatment efficacy. Unrealistic treatment expectations and critical views on medication in general have been found to predict lack of persistence. However, as MS treatments are only partially effective, perceived lack of efficacy sometimes overlaps with objective breakthrough disease. In addition, other psychological factors such as depression, self-efficacy, hope, and physician trust play a role in adherence.<sup>10</sup> Interestingly, Riñón et al.<sup>11</sup> found substantial differences between patients' and physicians' perceptions of adherence. Although patients commonly reported non-adherence, 59% of physicians did not consider adherence to be a problem.

Little research has been undertaken in the area of adherence to rehabilitative interventions or symptom-oriented drug treatments in MS. The same holds true for behavioural interventions addressing psychological, neuropsychological, or psychiatric symptoms in MS.

In MS, very few systematic studies have investigated the effectiveness of adherence interventions. Perceived efficacy and side effects should be priority areas to address in intervention studies, given their known association with treatment adherence in MS. The timely use of carefully developed and administered evidence-based educational tools might be the best approach to prevent misplaced expectations and to reach agreement on medication efficacy between patients and physicians. A recent trial has shown that this approach might increase adherence.<sup>12</sup>

Injection aids, co-medications, and alternative oral immunotherapies are now available to ameliorate or eliminate injection site reactions. Information and low-barrier access to expert support may also aid adherence. However, even with the most elaborate interventions, problems may persist. Pilot work utilizing motivational interviewing, a collaborate style of talk therapy that respects the patient's perspectives and encourages autonomy, is currently underway. Having demonstrated some success improving adherence

**Table 1.** Research questions and approaches.

<p><b>Understanding medicines use – people with MS and informal caregivers</b></p> <ul style="list-style-type: none"> <li>• Understanding patient decision-making, treatment practice and factors shaping adherence to treatment in socio-demographic context and longitudinally.</li> <li>• To what extent do people with MS adhere or non-adhere at different points in time across the trajectory of disease, and what predicts that non-adherence?</li> <li>• What motivates or influences patients to switch disease-modifying treatments?</li> <li>• Understanding the impact of co-morbidities.</li> <li>• What is the range of ways in which informal caregivers (family members, partners, friends, relatives) support patients with MS with medicines?</li> </ul> <p><b>Understanding medicines use – the role of healthcare professionals</b></p> <ul style="list-style-type: none"> <li>• Clarify characteristics of direct care (neurologists, nurses, general medical practitioners) and allied care (pharmacists, psychologists, physical/occupational therapists) health professionals that support adherence.</li> </ul> <p><b>Understanding medicines use – current practice and processes</b></p> <ul style="list-style-type: none"> <li>• Reviewing and synthesizing treatment practices and approaches across different countries.</li> </ul> <p><b>Behaviour change interventions to support medicines adherence</b></p> <ul style="list-style-type: none"> <li>• Plan and conduct trials comparing patient information leaflets and patient decision aids and their impact on patient adherence (and the context and effectiveness of their use).</li> <li>• Does MS self-management training influence adherence with treatment?</li> <li>• Exploring the use of telehealth / mobile technologies and how they could enhance adherence with treatment.</li> <li>• Understanding how altered communication strategies in consultations between health professionals and MS patients shape patient adherence with treatment.</li> <li>• Does personalized feedback and counselling on medicines taking enhance adherence?</li> </ul>
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among patients with Human Immunodeficiency Virus,<sup>13</sup> motivational interviewing may also increase healthcare utilization among MS patients who prematurely discontinue treatments.<sup>14</sup>

### Focus group results

The focus group outlined a diverse range of research questions and approaches around use of medicines. Although there was no clear consensus on a research agenda, four different domains for research emerged (details are given in Table 1):

1. Focussing the patient and their informal team
2. Describing the role of health professionals
3. Reviewing the evidence
4. Testing new interventions

These topics need to be examined in a rigorous way as part of a sustained collaborative effort. In addition, survey work might be useful to engage a larger community of health experts as well as patients and other stakeholders.

### Conclusions

Participants agreed on the term ‘adherence’ as most appropriate for use in MS. It was also agreed that treatment adherence is a major issue in MS and systematic approaches to describe, assess and modify adherence patterns are needed. Because adherence starts with the decision to change a health behaviour, understanding

patients’ preferences and needs is of the utmost importance. Physicians can lack insight about what their patients value and prefer.<sup>13</sup> Providing education and establishing patient preferences for treatment may be an appropriate starting point. The NICE guidelines on adherence<sup>14</sup> strongly advocate for patient involvement in decision-making about treatments to support medication adherence. Furthermore, major emphasis is placed on routinely assessing non-adherence as a common problem in a non-judgemental way. To summarize, whilst efficacious medical and behavioural interventions and products for MS are increasingly available, researchers need to develop a better understanding of how patients can consistently utilize health resources. Adherence to interventions not drug-related was not discussed in detail, and will be the focus in a second meeting.

### Participants

Three neurologists (JSG, AS, CH), three psychologists (LE, JB, WC), one sociologist (PB), two MS nurse specialists (ARP, VM), one physiotherapist (PF), one health scientist (SK), one rehab scientist (MA), three patient representatives, one patient advocate and five industry representatives.

### Conflict of interest

CH has received speaker honoraria from Biogen Idec, Genzyme. He has received study grant for MS health care research from Novartis Pharma, Biogen Idec.

JB has received funding, consulting fees, and/or honorarium from the National Multiple Sclerosis Society, Cephalon, the Novartis MS and Cognition Medical Advisory Board, the National Hockey League, Princeton University, the University of Missouri Research Board, and the National Institutes of Health. He is also a member of the Novartis Unbranded Speaker's Bureau.

PF was an advisory board member for Biogen Idec and Novartis, and has received speaker honoraria from Serono Foundation.

JSG has served in advisory boards of Biogen and Novartis and as speaker for Genzyme, Merck-Serono, TEVA and Novartis.

AS was a board member for Biogen Idec and Novartis, and has received speaker honoraria from Genzyme, Merck Serono, and Serono Foundation.

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